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Structural and functional studies of the tryptic core of the human chorionic gonadotropin beta-subunit.

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The beta-subunit of hCG was digested with trypsin to produce a modified form of the subunit for structure-function and immunological studies. After digestion of hCG beta with trypsin, the residual disulfide-linked core was isolated and found to be lacking the carboxy-terminal peptide (residues 115-145) and to contain bond cleavages between residues 2-3, 43-44, 74-75, and 95-96. The locations of these bond cleavages within the disulfide-bridged core were identified by isolation of the following peptides after reduction and S-carboxymethylation of the trypsin beta-core: beta 1-43, beta 3-43, beta 44-74, beta 44-95, beta 75-95, and beta 96-114. The circular dichroic spectrum of the tryptic beta-core over the wavelength region of about 200-320 nm was similar to that of the native subunit. In addition, the tryptic beta-core retained nearly full immunopotency in both polyclonal and monoclonal competitive RIAs and could combine with complementary native alpha-subunit. The hybrid, composed of the tryptic beta-core and native alpha, was purified and displayed a molar potency of about 0.1% relative to intact hCG in both a radioreceptor assay and an adenylate cyclase assay. Thus, the hybrid retained little biological activity. Although the extensive bond cleavages in the tryptic beta-core did not appear to change its secondary and tertiary structure sufficiently to significantly alter the circular dichroic spectrum, the immunoreactivity, or the capability to combine with its alpha-subunit complement, the biological functional integrity of the tryptic beta-core-containing hybrid was essentially abolished. Hence, the tryptic beta-core provides a useful derivative for detailed structure-function studies aimed at defining the necessary determinants for subunit association, receptor binding, and subsequent biological actions.

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